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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,847	08/04/2003	Neil J. Bulleid	39-286	5853

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EXAMINER	
HILL, KEVIN KAI	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
08/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,847	BULLEID, NEIL J.	
	Examiner	Art Unit	
	KEVIN K. HILL	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-47* is/are pending in the application.

4a) Of the above claim(s) *45-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action
Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2007 has been entered.

Election/Restrictions

Applicant has elected with traverse the invention of Group I, Claims 29-44, drawn to a method of producing pro-collagen comprising expressing a nucleic acid in an isolated cell.

Claims 28-44 are under consideration.

Priority

This application is a continuation of application 09/380,377, filed September 16, 1999, which is a 371 application of PCT/GB98/00468, filed March 2, 1998. Applicant's claim for the benefit of a prior-filed application 09/380,377 under 35 U.S.C. 119(e) and PCT/GB98/O0468 under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Acknowledgment is also made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy of UK 9704305.3, filed March 1, 1997, has been filed in parent application 09/380,377, filed September 16, 1999.

Accordingly, the effective priority date of the instant application is granted as March 1, 1997.

In the amendment filed June 11, 2007, Applicant has amended the Sequence Listing of SEQ ID NO:6 to be in accordance with the sequence presented in the specification (pg 5, line 12 and Figure 13). Support for the amended SEQ ID NO:6 is found in Figure 13 of application 09/380377, filed September 16, 1999.

Accordingly, the effective priority date of claim 34 is granted as March 1, 1997.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. **Claims 28-37 and 39-43 stand rejected on the ground of nonstatutory obviousness-type double patenting** as being unpatentable over claims 1-3, 5-6, 12-13 and 17-19 of Bulleid et al, U.S. Patent No. 6,171,827 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method and materials to perform said method claimed in the instant application are encompassed by the patented method(s) and patented materials to perform said patented method(s).

With respect to Claim 28 of the instant application, Applicant claims a method for producing a first pro-collagen in a cell, wherein a nucleic acid sequence encodes a first pro-alpha chain for assembly into said first pro-collagen, wherein said first pro-collagen does not assemble with a second pro-collagen expressed in said cell, and wherein the first pro-collagen comprises a first moiety having activity for assembly into a trimeric pro-collagen C-propeptide, contains a recognition sequence for chain selection, and a second moiety containing a triple helix-forming domain from a pro-alpha chain different from said first type of pro-alpha chain.

Bulleid et al, in claims 12, 13 and 19, recite methods for producing a collagen comprising the production of a pro-collagen polypeptide having a first moiety having activity for assembly into a trimeric pro-collagen C-propeptide and being from a first type of pro-alpha chain, wherein said first moiety contains a recognition sequence for chain selection, and a second moiety containing a triple helix-forming domain from a pro-alpha chain different from said first type of pro-alpha chain. The methods comprise the use of the polypeptide(s) claimed in claims 1-3 and 5-6, the DNA molecule(s) claimed in claim 17, and the expression host cell(s) claimed in claim 18.

Thus, it would be obvious to one of ordinary skill in the art that the method(s) of Bulleid et al are designed to achieve the same results as the method of the instant application, and thus reasonably encompass the instantly claimed invention.

With respect to Claims 29-36 of the instant application, Applicant claims the recognition sequence of the first moiety of the first type of pro-alpha collagen chain to comprise the amino acid sequence shown in SEQ ID NO: 1-8.

Bulleid et al, in claim 3, recite that the recognition sequence of the first moiety of the first type of pro-alpha collagen chain to comprise the amino acid sequence shown in SEQ ID NO: 6-13.

Because both Applicant and Bulleid et al use the generic terms "SEQ ID NO" in their claim language, the Examiner has looked to the specification for definition(s) to better understand the nature of the invention. Upon examination of the respective amino acid sequences of SEQ ID NO: 1-8 of the instant application and SEQ ID NO: 6-13 of Bulleid et al, the following correlations between the instant application SEQ ID NO's and the SEQ ID NO's of Bulleid et al are readily apparent, wherein:

SEQ ID NO:1 is identical to SEQ ID NO:7,
SEQ ID NO:2 is identical to SEQ ID NO:8,
SEQ ID NO:3 is identical to SEQ ID NO:9,
SEQ ID NO:4 is identical to SEQ ID NO:6,
SEQ ID NO:5 is identical to SEQ ID NO:10,
SEQ ID NO:7 is identical to SEQ ID NO:12, and
SEQ ID NO:8 is identical to SEQ ID NO:13.

Thus, it would be obvious to one of ordinary skill in the art that the patented recognition sequences of SEQ ID NO: 6-10 and 12-13 reasonably embrace the instantly claimed recognition sequences of SEQ ID NO: 1-5 and 7-8 recited in Claims 29-33 and 35-36.

SEQ ID NO:6 is identical to SEQ ID NO:11, except for position 10, wherein the Leucine (Leu) of SEQ ID NO:11 is substituted with Isoleucine (Ile) in SEQ ID NO:6. However, the art generally recognizes the substitution of Leucine for Isoleucine to be functionally conservative. Absent evidence to the contrary and a showing of unexpected results, it would be obvious to one of ordinary skill in the art that the patented recognition sequence of SEQ ID NO: 11 anticipates the genus of amino acid sequences identical to SEQ ID NO:11 wherein the amino acid at position 10 may be substituted for another naturally-occurring amino acid, and thus SEQ ID NO:11 reasonably embraces the instantly claimed recognition sequence of SEQ ID NO:6.

With respect to Claim 37 of the instant application, Applicant claims the first and second types of pro-alpha collagen chains to be selected from the group consisting of the pro-alpha 1(I), pro-alpha 2(I), pro-alpha 1(II), pro-alpha 1(III), pro-alpha 1(V), pro-alpha 2(V), pro-alpha 1(XI) and pro-alpha 2(XI).

Bulleid et al, in claims 2 and 6, recite that the first and second moieties from a first type and second type of pro-alpha collagen chain has a recognition sequence selected from the group consisting of the pro-alpha 1(I), pro-alpha 2(I), pro-alpha 1(II), pro-alpha 1(III), pro-alpha 1(V), pro-alpha 2(V), pro-alpha 1(XI) and pro-alpha 2(XI).

Thus, it would be obvious to one of ordinary skill in the art that the patented pro-alpha collagen chains from which the first and second moieties containing a triple helix-forming domain are obtained reasonably embrace the instantly claimed first and second types of pro-alpha collagen chains recited in Claim 37.

With respect to Claims 39-40 of the instant application, Applicant claims a nucleic acid sequence encoding pro-alpha collagen chains to be incorporated into a plasmid, cosmid or phage vector.

Bulleid et al, in claims 17-18, recite a DNA molecule encoding the polypeptide having activity for assembly into a trimeric pro-collagen C-propeptide, wherein the nucleic acid is operably linked to a regulatory sequence that directs expression of said polypeptide. Because Bulleid et al use the generic term "DNA molecule", the Examiner has looked to the specification to better understand the nature of the invention. Bulleid et al disclose that the recombinant DNA in accordance with the invention may be in the form of a vector. The vector may be, for example, a plasmid, cosmid or phage (column 5, lines 47-49).

Thus, it would be obvious to one of ordinary skill in the art that the genus of DNA molecule(s) contemplated by Bulleid et al reasonably embrace the instantly recited vector nucleic acid molecules.

With respect to Claims 41-43 of the instant application, Applicant claims the cell expressing the nucleic acid molecule encoding the pro-collagen molecule to be a eukaryotic cell, e.g. yeast, insect or a mammalian cell.

Bulleid et al, in claim 18, recite a host cell for expressing the DNA molecule encoding the inventive pro-collagen molecule. Because Bulleid et al use the generic term "expression host cell", the Examiner has looked to the specification to better understand the nature of the invention. Bulleid et al disclose that the expression host cell may be eukaryotic, including yeasts, insects and mammalian cell lines (column 5, lines 64-66).

Thus, it would be obvious to one of ordinary skill in the art that the genus of expression host cells contemplated by Bulleid et al reasonably embrace the instantly recited host cells.

Therefore, claims 1-3, 5-6, 12-13 and 17-19 of U.S. Patent No. 6,171,827 B1 anticipate the Claims 28-37 and 39-43 in the instant application.

Applicant's Arguments

Applicant argues that:

a) the claims of U.S. Patent No. 6,171,827 B1 does not teach that a first procollagen be produced in a cell that expresses and assembles a second procollagen; and

b) the present claims require the expression in the cell of nucleic acid sequence(s) that encode(s) a pro-α chain for assembly into the first procollagen, which nucleic acid sequence(s) do/does not encode pro-α chain(s) that co-assemble with the pro-α chains that assemble to form the second procollagen. Clearly, nothing in the cited patent claims are suggestive of this further requirement.

Applicant's argument(s) has been fully considered, but is not persuasive.

With respect to a), Applicant's attention is drawn to claim 19 of U.S. Patent No. 6,171,827 B1, wherein the method of producing a collagen is performed in a cell, wherein Bulleid et al disclose that the expression host cell may be eukaryotic, including yeasts, insects and mammalian cell lines (column 5, lines 64-66). Applicant has provided no evidence that the eukaryotic cell types, e.g. mammalian cells, contemplated by Bulleid et al (column 5, lines 64-66) would not inherently express an endogenous pro-collagen molecule or specifically exclude those eukaryotic cells that express a [endogenous] second procollagen for use in the inventive method.

With respect to b), the pro-α chains recited in the U.S. Patent No. 6,171,827 B1 are the same as the pro-α chains recited in the instant application, and thus the functional limitation that the pro-α chain does not co-assemble with pro-α chains that assemble to form said second collagen is an inherent feature of the claimed pro-α chains. Although the functional properties of the pro-α chains are recited in the instant application, the patented pro-α chains used in the patented method are structurally the same, or in the case of SEQ ID NO:6 (instant)/SEQ ID NO:11(patent) substantially similar to, the instantly recited pro-α chains used in the instantly recited method. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Applicant has provided no evidence that the patented pro-α chains used in the patented method would not possess the instantly recited functional properties.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the Applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

2. **Claims 28-33 and 35-43 stand rejected under 35 U.S.C. 102(e)** as being anticipated by Bulleid et al (U.S. Patent No. 6,171,827 B1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

With respect to Claim 28, Bulleid et al teach the production of novel collagens in which combinations of alpha chains which are not seen in nature because of the assembly-directing effect of the natural C-propeptides (column 4, lines 49-56). The invention allows the protein engineer to construct novel collagens having a non-natural combination of alpha chains (columns 3-5). The inventive pro-collagen molecules may be expressed from a recombinant DNA system and transformed/transfected into a host expression cell (column 5, lines 40-66).

With respect to Claims 29-33 and 35-36, Bulleid et al teach the recognition sequences having the amino acid sequences of SEQ ID NO: 6-13 (column 8, lines 24-27), wherein SEQ ID

NO:1 is identical to SEQ ID NO:7, SEQ ID NO:2 is identical to SEQ ID NO:8, SEQ ID NO:3 is identical to SEQ ID NO:9, SEQ ID NO:4 is identical to SEQ ID NO:6, SEQ ID NO:5 is identical to SEQ ID NO:10, SEQ ID NO:7 is identical to SEQ ID NO:12, and SEQ ID NO:8 is identical to SEQ ID NO:13.

With respect to Claims 37-38, Bulleid et al teach that the recognition site sequence may be, or substituted for, a recognition sequence selected from the group consisting of the pro-alpha 1(I), pro-alpha 2(I), pro-alpha 1(II), pro-alpha 1(III), pro-alpha 1(V), pro-alpha 2(V), pro-alpha 1(XI) and pro-alpha 2(XI) (column 3, lines 50-52; column 4, lines 7-8). Similarly, the second moiety may comprise at least a collagen alpha chain selected from the same group (column 4, lines 60-65).

With respect to Claims 39-40, Bulleid et al disclose that the recombinant DNA in accordance with the invention may be in the form of a vector. The vector may be, for example, a plasmid, cosmid or phage (column 5, lines 47-49).

With respect to Claims 41-43, Bulleid et al teach the expression host cell may be eukaryotic, including yeasts, insects and mammalian cell lines (column 5, lines 64-66).

Thus, Bulleid et al anticipate Claims 28-33 and 35-43.

Applicant's Arguments

Applicant argues that the Examiner appears to have overlooked the requirements in the instant claims relating to the nature of the host cells used and the nucleic acid sequence expressed. These requirements are not taught by citation.

Applicant's argument(s) has been fully considered, but is not persuasive. Bulleid et al teach cells transfected with a nucleic acid encoding a first procollagen molecule having the instantly recited structural properties, wherein said cells are used in a method of producing a first procollagen molecule. Applicant's terse statements do not shed light on how the instant application is clearly distinguished from Bulleid et al, nor how Bulleid et al, as a whole, specifically fail to teach the instantly claimed invention.

3. **Claims 28-33 and 35-43 stand rejected under 35 U.S.C. 102(f)** because the Applicant did not invent the claimed subject matter. The prior art reference (U.S. Patent No. 6,171,827 B1) establishes that two individuals, Neil Bulleid and Karl Kadler, are the inventors of the claimed subject matter.

Applicant's Arguments

Applicant argues that the rejection is based upon the Examiner's misunderstanding of the reference.

Applicant's argument(s) has been fully considered, but is not persuasive. It is incumbent upon the inventors named in the application, in reply to an inquiry regarding the appropriate inventorship under subsection (f), or to rebut a rejection under 35 U.S.C. 102(a) or (e), to

provide a satisfactory showing by way of affidavit under 37 CFR 1.132 that the inventorship of the application is correct in that the reference discloses subject matter invented by the Applicant rather than derived from the author or patentee notwithstanding the authorship of the article or the inventorship of the patent. In re Katz, 687 F.2d 450, 455, 215 USPQ 14, 18 (CCPA 1982) (inquiry is appropriate to clarify any ambiguity created by an article regarding inventorship, and it is then incumbent upon the Applicant to provide "a satisfactory showing that would lead to a reasonable conclusion that [Applicant] is the…inventor" of the subject matter disclosed in the article and claimed in the application). See MPEP 2137.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. **Claims 28-44 stand rejected under 35 U.S.C. 103(a)** as being obvious over Bulleid et al (U.S. Patent No. 6,171,827 B1), as evidenced by Barr et al (U.S. Patent No. 5,460,950).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Bulleid et al teach the production of novel collagens in which combinations of alpha chains which are not seen in nature because of the assembly-directing effect of the natural C-propeptides (column 4, lines 49-56). The recognition sequences necessary and sufficient to determine the type-specific assembly of the moieties to which it is attached may be a recognition sequence selected from the group consisting of the pro-alpha 1(I), pro-alpha 2(I), pro-alpha 1(II), pro-alpha 1(III), pro-alpha 1(V), pro-alpha 2(V), pro-alpha 1(XI) and pro-alpha 2(XI) (column 3, lines 50-52; column 4, lines 7-8) and have the amino acid sequences of SEQ ID NO: 6-13 (column 8, lines 24-27), wherein SEQ ID NO:1 is identical to SEQ ID NO:7, SEQ ID NO:2 is identical to SEQ ID NO:8, SEQ ID NO:3 is identical to SEQ ID NO:9, SEQ ID NO:4 is identical to SEQ ID NO:6, SEQ ID NO:5 is identical to SEQ ID NO:10, SEQ ID NO:7 is identical to SEQ ID NO:12, and SEQ ID NO:8 is identical to SEQ ID NO:13.

The invention allows the protein engineer to construct novel collagens having a non-natural combination of alpha chains (columns 3-5). The inventive pro-collagen molecules may be expressed from a recombinant DNA system and transformed/transfected into a host expression cell (column 5, lines 40-66), wherein such host cells may be eukaryotic cells, including yeasts, insects and mammalian cell lines.

Bulleid et al do not teach the use of BHK, 3T3, CHO and COS cells, as recited in Claim 44. However, at the time of filing of the instant application, the art recognized that these mammalian cell lines were generally useful for the expression of exogenous proteins (Barr et al, column 14, lines 7-35).

Bulleid et al also do not teach SEQ ID NO:6. However, SEQ ID NO:6 is identical to SEQ ID NO:11, except for position 10, wherein the Leucine (Leu) of SEQ ID NO:11 is substituted with Isoleucine (Ile) in SEQ ID NO:6.

It would have been obvious to one of ordinary skill in the art to modify the method of Bulleid et al with the method of the instant application with a reasonable chance of success because Bulleid et al disclose how an artisan may express and synthesize recombinant pro-collagen molecules that do not oligomerize with any pro-collagen molecules endogenously expressed in the given host cell. An artisan would be motivated to modify the method of Bulleid et al because the prior art teaches that the method(s) is useful for the synthesis and recovery of novel, non-naturally-occurring collagen molecules.

Absent evidence to the contrary and a showing of unexpected results, it also would have been obvious to one of ordinary skill in the art to modify the Leucine residue at position 10 of the recognition sequence of SEQ ID NO:11 with an Isoleucine with a reasonable chance of success because the art generally recognizes the substitution of Leucine for Isoleucine to be functionally conservative. Applicant discloses the prototypical C-propeptide motif which directs chain assembly (pg 25, Section 2.3), wherein the most divergent residues are underscored. It is noted that the Leucine/Isoleucine residue at issue is encompassed within this most divergent motif. An artisan would be motivated to substitute amino acids of SEQ ID NO:11 because some amino acids in the recognition sequence are less well conserved than others but may form a core-recognition sequence that is of critical importance in the selection process, and thus modification of any given amino acid will be advantageous in the optimization of the inventive recognition site so as to promote trimerization with a desired pro-collagen molecule and inability to trimerize with a non-desired pro-collagen molecule simultaneously expressed in the given host cell.

Thus, the invention as a whole is *prima facie* obvious.

Applicant's Arguments

Applicant argues that nothing in Barr et al cures the deficiency of Bulleid et al.

Applicant's argument(s) has been fully considered, but is not persuasive. The Examiner's response to what is taught by Bulleid et al is discussed above, and is incorporated herein. Barr et al is applied for teaching that the art recognized BHK, 3T3, CHO and COS cells, as recited in Claim 44, were generally useful for the expression of exogenous proteins (Barr et al, column 14, lines 7-35).

Conclusion

5. No claims are allowed.

This is a continuation of Applicant's earlier Application No. 10/632,847. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill, Ph.D./
Examiner, Art Unit 1633

/Q. JANICE LI, M.D./
Primary Examiner, Art Unit 1633